How to Get Devices Approved

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Office of Devices Evaluation
Center of Devices and Radiological Health (CDRH)
Utilize all available CDRH resources.
CDRH Learn

- Innovative educational tool
- Consists of learning modules describing many aspects of medical device regulations
- Intended to provide industry with information that is comprehensive, interactive, and easily accessible
- Various formats, including videos, audio recordings, and slide presentations

www.fda.gov/Training/CDRHLearn/default.htm
It is a Medical Device if it:

• Diagnoses, Cures, Mitigates, Treats or Prevents a Disease or Condition, or

• Affects the Function or Structure or the Body, and

• Does Not Achieve Intended Use Through Chemical Action, and

• Is Not Metabolized
CDRH- Device Classification

- Devices are classified into Class I, II, or III
- Device classification is based on the controls necessary to provide a reasonable assurance of safety and effectiveness:
  - Class I – General Controls are sufficient
    - Most Class I Devices are also exempt from premarket notification
  - Class II – General Controls and Special Controls are required (Typically require 510(k))
  - Class III – General controls and Premarket Approval are required (Typically require PMA)
# Ophthalmic Examples

<table>
<thead>
<tr>
<th>CLASS I</th>
<th>CLASS II</th>
<th>CLASS III</th>
</tr>
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<tbody>
<tr>
<td>VA chart</td>
<td>Daily wear CL</td>
<td>IOLs</td>
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<tr>
<td>Perimeter</td>
<td>Vitrectomy instruments</td>
<td>Excimers</td>
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<tr>
<td>Topographer</td>
<td>Phaco instruments</td>
<td>Viscoelastics</td>
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<tr>
<td></td>
<td></td>
<td>Endotamponades</td>
</tr>
</tbody>
</table>
FDA Resources

• Device Classification
  www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm

• Request for Information (513(g))
  » Means for obtaining the agency's views about the classification/regulatory requirements that may be applicable to a particular device
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm209841.htm
## Premarket Applications for Devices

<table>
<thead>
<tr>
<th>Application Type</th>
<th>Review Standard</th>
<th>Applies To:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premarket Notification [510(k)]</td>
<td>Substantial Equivalence</td>
<td>Class II devices (some Class I)</td>
</tr>
<tr>
<td>Premarket Approval (PMA)</td>
<td>Reasonable assurance of safety and effectiveness</td>
<td>Class III devices</td>
</tr>
<tr>
<td>Humanitarian Device Exemptions (HDE)</td>
<td>Safety and probable benefit</td>
<td>Devices for small populations</td>
</tr>
</tbody>
</table>
The SPECTRALIS is a non-contact ophthalmic diagnostic imaging device. It is intended for viewing the posterior segment of the eye, including two- and three-dimensional imaging, cross-sectional imaging (SPECTRALIS HRA+OCT and SPECTRALIS OCT), fundus photography, fluorescence imaging (fluorescein angiography, indocyanine green angiography; SPECTRALIS HRA+OCT, SPECTRALIS HRA), autofluorescence imaging (SPECTRALIS HRA+OCT, SPECTRALIS HRA and SPECTRALIS OCT BluePeak) and to perform measurements of ocular anatomy and ocular lesions. The device is indicated as an aid in the detection and management of various ocular diseases, including age-related macular degeneration, macular edema, diabetic retinopathy, retinal and choroidal vascular diseases, glaucoma, and for viewing geographic atrophy as well as changes in the eye that result from neurodegenerative diseases. The SPECTRALIS HRA+OCT and SPECTRALIS OCT include normative databases for retinal nerve fiber layer thickness and optic nerve head neuroretinal parameter measurements, which are used to quantitatively compare the retinal nerve fiber layer and neuroretinal rim in the human retina to values found in normal subjects.”
PMA Example

- Extended depth of focus (EDF) optical technology for providing an extended range of vision
  » **TECNIS® Symfony IOL**; +5.0D to +34.0D. (P98040/S065) – 7/15/2016

EDF optical technology for patients with astigmatism; 1.5D to 6.0D cylinder power

http://www.tecnisiol.com/eu/tecnis-symfony-iol.htm

http://www.eyetreatmentcenter.com/services-cataracts/astigmatism-correction
Humanitarian Device Exemption (HDE)

• For diseases/conditions affecting < 4000 individuals in the U.S. per year

• HDE must show:
  » Does not pose unreasonable risk of illness or injury (i.e., safety is demonstrated), AND
  » Probable benefit outweighs the risk (i.e., exempt from effectiveness requirements of a PMA)
Argus II Retinal Prosthesis System: H110002

Implantable retinal prosthesis Subsystem

- Retinal prosthesis
  - electronic package with suture tab
  - 60 electrode array
  - scleral band

- Retinal tack

- Glasses with video camera & coil antenna

- Video Processing Unit (VPU)

Externals

- Laptop & software

Clinician Fitting System
FDA Resources: Summaries

• Summary of Safety and Effectiveness
  • http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm

• Summary of Safety and Probable Benefit
  • http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm

• 510(k) Summaries
  • http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/default.htm
De Novo

• Establishes a new “device type” along with classification, regulation, and product code

• Established in 1997 (FDAMA)

• Modified in 2012 to streamline and increase efficiency in process (FDASIA):
  » Removed requirement for sponsor to submit 510(k) prior to submission of de novo request.
  » Created two pathways for de novo submissions: post-510(k) NSE and direct de novo.
  » Timeframe for review set at 120 days

• De Novo Draft Guidance - 2014
Recent Ophthalmic De Novo’s

- Diurnal pattern recorder system to monitor IOP fluctuations
  - Sensimed Triggerfish from Sensimed AG (DEN140017) – 3/4/16

- Nasolacrimal compression device to reduce drainage
  - Tear Duct Occluder from Innovatex, Inc. (DEN140022) – 4/20/16

- Automated detection device for amblyopia in children 2 to 8
  - Pediatric Vision Scanner from RebiScan, Inc. (DEN130051) – 6/8/16
FDA Resources: Guidance

- Guidance describes FDA’s interpretation of, or policy on, a regulatory issue
  - Submissions
  - Labeling
  - Manufacturing

- Guidance for Clinical Studies
  - Regulatory Pathway
  - Study Design
  - Data Analysis

- Check availability of FDA Guidance
  www.fda.gov/cdrh/guidance.html
“Leap-Frog” Guidance

• Mechanism via which we can share our initial thoughts regarding the content of premarket submissions for emerging technologies:
  » Speed development and approval of future submissions

• Retinal Prosthesis
  • http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm341954.htm

• Minimally Invasive Glaucoma Devices
FDA Resources: Recognized Standards

• A consensus standard which FDA has recognized for use in satisfying a premarket submission requirement

• Outlines:
  » Parameters needed for evaluation of a specific device
  » Pre-clinical testing needed prior to human testing
  » Recommended clinical trial

• Check recognized Standards

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
# Example: ANSI / ASTM Ophthalmic Recognized Standards

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANSI</td>
<td>Z80.10-2009</td>
<td>Ophthalmic Instruments -- Tonometers</td>
</tr>
<tr>
<td>ANSI</td>
<td>Z80.18-2010</td>
<td>American National Standard for Ophthalmics - Contact Lens Care Products - Vocabulary, Performance Specifications and Test Methodology</td>
</tr>
<tr>
<td>ANSI</td>
<td>Z80.21-2010</td>
<td>American National Standard for Ophthalmics - Instruments - General - Purpose Clinical Visual Acuity Charts</td>
</tr>
<tr>
<td>ANSI</td>
<td>Z80.11-2012</td>
<td>American National Standard for Ophthalmics - Laser Systems for Corneal Reshaping</td>
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<tr>
<td>ANSI</td>
<td>Z80.7-2013</td>
<td>Ophthalmics - Intraocular Lenses</td>
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<tr>
<td>ANSI</td>
<td>Z80.20-2010</td>
<td>American National Standard for Ophthalmics - Contact Lenses - Standard Terminology, Tolerances, Measurements and Physical Properties</td>
</tr>
<tr>
<td>ANSI</td>
<td>Z80.27-2014</td>
<td>American National Standard for Ophthalmics - Implantable Glaucoma Devices</td>
</tr>
<tr>
<td>ASTM</td>
<td>D882-12</td>
<td>Standard Test Methods for Tensile Properties of Thin Plastic Sheeting</td>
</tr>
<tr>
<td>ASTM</td>
<td>D790-10</td>
<td>Standard Test Methods for Flexure Properties of Unreinforced Plastics and Electrical Insulating Materials</td>
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</table>
## ISO Ophthalmic Recognized Standards

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<tr>
<th>Type</th>
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<th>Name</th>
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<tbody>
<tr>
<td>ISO</td>
<td>14730</td>
<td>First edition 2000-09-15 Ophthalmic optics -- Contact lens care products -- Antimicrobial preservative efficacy testing and guidance on determining discard date</td>
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<tr>
<td>ISO</td>
<td>10939</td>
<td>Second edition 2007-02-01 Ophthalmic instruments -- Slit-lamp microscopes</td>
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<tr>
<td>ISO</td>
<td>10942</td>
<td>Second edition 2006-06-01 Ophthalmic instruments -- Direct ophthalmoscopes</td>
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<tr>
<td>ISO</td>
<td>15004-1</td>
<td>First edition 2006-06-01 Ophthalmic instruments - Fundamental requirements and test methods - Part 1: General requirements applicable to all ophthalmic instruments</td>
</tr>
<tr>
<td>ISO</td>
<td>9394</td>
<td>Third edition 2012-10-01 Ophthalmic optics -- Contact lenses and contact lens care products -- Determination of biocompatibility by ocular study with rabbit eyes</td>
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<tr>
<td>ISO</td>
<td>12865</td>
<td>Second edition 2006-07-01 Ophthalmic instruments -- Retinoscopes</td>
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<tr>
<td>ISO</td>
<td>18369-4</td>
<td>First edition 2006-08-15 Ophthalmic optics - contact lenses - Part 4: Physicochemical properties of contact lens materials</td>
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<tr>
<td>ISO</td>
<td>11981</td>
<td>Second edition 2009-07-01 Ophthalmic optics -- Contact lenses and contact lens care products -- Determination of physical compatibility of contact lens care products with contact lenses</td>
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<tr>
<td>ISO</td>
<td>TR 22979</td>
<td>First edition 2006-02-01 Ophthalmic implants - Intraocular lenses - Guidance on assessment of the need for clinical investigation or intraocular lens design modifications</td>
</tr>
<tr>
<td>ISO</td>
<td>15752</td>
<td>Second edition 2010-01-15 Ophthalmic instruments - Endoilluminators - Fundamental requirements and test for optical radiation safety</td>
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<tr>
<td>ISO</td>
<td>10936-2</td>
<td>Second edition 2010-01-15 Optics and photonics - Operation microscopes - Part 2: Light hazard from operation microscopes used in ocular surgery</td>
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<tr>
<td>ISO</td>
<td>11986</td>
<td>Second edition 2010-11-01 Ophthalmic optics -- Contact lenses and contact lens care products -- Guidelines for determination of preservation uptake and release</td>
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<tr>
<td>ISO</td>
<td>10943</td>
<td>Third edition 2011-08-15 Ophthalmic instruments -- Indirect ophthalmoscopes</td>
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<tr>
<td>ISO</td>
<td>10940</td>
<td>Second edition 2009-08-01 Ophthalmic instruments - Fundus Cameras</td>
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<tr>
<td>ISO</td>
<td>11979-3</td>
<td>Third edition 2012-12-01 Ophthalmic implants -- Intraocular lenses -- Part 3: Mechanical properties and test methods</td>
</tr>
<tr>
<td>ISO</td>
<td>18369-2</td>
<td>Second edition 2012-12-01 Ophthalmic optics -- Contact lenses -- Part 2: Tolerances</td>
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<tr>
<td>ISO</td>
<td>11980</td>
<td>Third edition 2012-11-15 Ophthalmic optics - Contact lenses and contact lens care products -- Guidance for clinical investigations</td>
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<tr>
<td>ISO</td>
<td>14729</td>
<td>First edition 2001-04-15 Ophthalmic optics - Contact lens care products - Microbiological requirements and test methods for products and regimens for hygienic management of contact lenses [Including: Amendment 1 (2010)]</td>
</tr>
</tbody>
</table>
Investigational Device Exemptions (IDE)

- Allows investigational devices to be potentially used in clinical studies to support PMA, 510(k)
- Requirements for informed consent, labeling, monitoring, records/reports
- Requires approval by Institutional Review Board (IRB) and, for significant risk devices, FDA
- 30-day review period – if no action by FDA in 30 days, it is “deemed approved”
IDE

- Significant Risk Study - can not begin until IDE is approved by FDA
- Non Significant Risk (NSR) - no IDE submission to FDA
  - Abbreviated requirements (labeling, IRB, consent, monitoring, reporting, prohibition on promotion)
  - IRB serves as the FDA’s surrogate for review, approval, and continuing review of the NSR device studies.
  - An NSR device study may start at the institution as soon as the IRB reviews and approves the study
Significant Risk (SR) Study

• Presents a potential for serious risk to the health, safety, and welfare of a subject and is:
  » an implant; or
  » used in supporting or sustaining human life; or
  » of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health
  » otherwise poses a risk
Early Feasibility Study Program

• **Goal** - Encouraging innovation in the US by supporting the study of new technology

• **Elements:**
  » Small number of subjects
  » Device that may be early in development, typically before the device design has been finalized
  » Usually the first clinical use of the device for the proposed indications for use
Early Feasibility Study Program

• Guidance –

• Key Principle - Approval of an early feasibility study IDE may be based on less nonclinical data than would be needed to support the initiation of a larger clinical study on a more final device design

• JAMA Ophthalmology -

• DOED contact - DOED_EFS@fda.hhs.gov
Plan Well

• “By failing to prepare, you are preparing to fail.” [Benjamin Franklin]

• “It does not do to leave a live dragon out of your calculations, if you live near him.” [J.R.R. Tolkien, The Hobbit]
  – Ask DOED during presubmissions the most complicated issues you are struggling with
Pre-Submission Program

• Facilitates device development / innovation by providing informal FDA feedback on proposed:
  » Preclinical testing
  » Clinical trial design (e.g., endpoints, inclusion/exclusion criteria, statistical analysis plan)
  » Proposed indications for use

• Provides an opportunity for a meeting with the FDA
  » Within 75 calendar days

The benefit of hindsight?
Consider Incorporating Patient Voice
Where can patient perspectives inform Medical Device development and evaluation?

- **Patient-Centered Outcomes**
- **Patient Preference Benefit-Risk Information**
- **Communicating Benefit-Risk Information to Patients**
- **Patient-Informed Clinical Trial Design, Patient Reported Outcomes**
- **Patient-Informed Needs**

**Stages of Development:**
- **Discovery + Ideation**
- **Invention + Prototyping**
- **Pre-Clinical**
- **Clinical**
- **Regulatory Decision**
- **Product Launch**
- **Post-Market Monitoring**
Partner with Patients

We interact with patients as partners and work together to advance the development and evaluation of innovative devices, and monitor the performance of marketed devices.

1. Promote a culture of meaningful patient engagement by facilitating CDRH interaction with patients.

2. Increase use and transparency of patient input as evidence in our decision-making.
What can PROs and PPI tell us?

Patient Reported Outcomes (PRO)
- Endpoints in regulatory studies
- Outcomes to monitor postmarket
- Interest to payers, providers, patients

Patient Preference Information (PPI)
- Inform endpoints or effect size for regulatory studies
- Inform subgroup considerations
- Labeling changes / expanded indications

PPI Guidance – Voluntary Submission, Review in PMAs / HDEs/ De Novos...
Collaborate to Advance Regulatory Science

Patients

Academic Centers

FDA

Industry

Professional Organizations (Providers)
Network of Experts

- Vetted network of outside scientists, clinicians and engineers who provide CDRH with rapid access to scientific, engineering, and medical expertise when it is needed to supplement existing knowledge and expertise within the CDRH

- Built on a series of agreements with external professional scientific and medical organizations
  
  » Currently enrolled organizations:
  
  http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/ucm289534.htm
Established partnerships with 11 organizations with expertise relevant to the review of ophthalmic devices:

1. American Academy of Ophthalmology
2. American Academy of Optometry
3. American Chemical Society
4. American-European Congress of Ophthalmic Surgery
5. American Glaucoma Society
6. American Optometric Association
7. Association for Research in Vision and Ophthalmology
8. American Society of Cataract and Refractive Surgery
9. American Society of Microbiology
10. American Society of Retina Specialists
11. American Veterinary Medicine Association
Process Overview
Developing Novel Endpoints
National Eye Institute/ FDA Clinical Trial Endpoints Symposia

• Glaucoma Clinical Drug Trial Design and Endpoints Symposium - 3/08
  http://www.iovs.org/content/50/4/1497.short

• Use of Patient-Reported Outcomes in Medical Product Development - 10/09
  http://www.iovs.org/content/51/12/6095.short

• Clinical Trial Design and Endpoints Symposium: Measures of Structural Change and Visual Function - 9/10
  http://www.iovs.org/content/52/11/7842.short

• Use of Functional Vision Endpoints in Visual Prostheses Development - 5/11
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm267127.htm

• Inflammatory Eye Disease - 3/15
  http://www.arvo.org/endpoints2015/

• Diabetic Retinopathy - 6/15
  http://www.arvo.org/DRconference/
Age-related macular degeneration (AMD) and inherited diseases

- Joint effort of FDA, NEI, ARVO & FFD
- AMD and inherited retinal diseases (IRDs)
- NOV 09, 2016
- National Institutes of Health (NIH) Campus
  Lister Hill Center
  Bethesda, MD.

Recent Workshops

• FDA/AGS Workshop on the Validity, Reliability, and Usability of Glaucoma Imaging Devices (Oct 5, 2012) http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm318305.htm

• FDA/AGS Workshop on Supporting Innovation for Safe and Effective Minimally Invasive Glaucoma Surgery (February 26, 2014)
  http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm382508.htm#webcast

• FDA/AAO Workshop on Developing Novel Endpoints for Premium Intraocular Lenses (March 24, 2014)
  http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm365646.htm

• FDA/AAO/AAOpt/AOA/CLAO Workshop on Revamping Microbiological Test Methods for Contact Lenses, Products, and Accessories to Protect Health and Ensure Safety (Sept 12, 2014)
  http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm409778.htm

• FDA/AAO/AAOpt/AAPOS/AOA/ASCRS/CLAO Workshop on Controlling the Progression of Myopia: Contact Lenses and Future Medical Devices (Sept 30, 2016)
  http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm500404.htm
AAO Task Force

• Subject Member Experts from AAO and FDA
• Industry Engagement
• AAO Task Force Consensus Statements Focusing on Device Innovation:
  • Adverse Event Definition for Safety and Performance Endpoints
  • Measurement of Tilt, Decentration and Chord Length
  • Specular Microscopy for Phakic IOLs
  • Testing for EDOF IOLs
  • Accommodation Clinical Studies for Accommodative IOLs
AAO Task Force on Novel Endpoints for Premium IOLs

AAO members:
• Chair, Jack Holladay, MD
• Adrian Glasser, PhD
• Scott MacRae, MD
• Samuel Masket, MD
• Walter Stark, MD

FDA members:
• Malvina Eydelman, MD
• Don Calogero, MS
• Gene Hilmantel, OD, MS
• Tieuvi Nguyen, PhD, RAC
• Eva Rorer, MD
• Michelle Tarver, MD, PhD
Task Force Deliverables

• Consensus statements published in Ophthalmology


5. The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events


http://www.aaojournal.org/inpress
Task Force Deliverables

✓ Consensus statements published in Ophthalmology

• Develop a psychometrically-evaluated PRO measure
  • Accepted into Pilot Program for Qualification of Medical Device Development Tools
Collaborate to fill gaps: AAO Task force

- Collaborative development with the FDA and the American Academy of Ophthalmology
- Industry consortium forming to develop tool
- PRO measure that assesses visual symptoms called dysphotopsias after receipt of a premium IOL (e.g., multifocal, extended depth of focus, accommodating, or toric lens)
Collaborate to Fill Gaps: LASIK Quality of Life Collaboration

- Patients with poor outcomes voiced concerns about LASIK
- Collaboration with Department of Defense (Navy Medical San Diego) and National Eye Institute
- Developed a tool to measure visual symptoms following LASIK surgery
Collaborate to Fill Gaps: UCSF/Stanford CERSI MIGS Project

- Collaboration with the UCSF/Stanford CERSI and the American Glaucoma Society
- Goal: To develop/modify a PROM sensitive to patients with mild to moderate glaucoma and able to detect change with device treatments
  - Convene panel of glaucoma specialists for input
  - Conduct focus groups to generate content
  - Develop a draft web-based questionnaire
  - Develop a protocol for evaluating the measurement properties of a newly created tool
Expedite Innovation

• Utilize all available FDA resources
• Maximize quality of premarket submissions
• Plan well
• Ask for FDA input early in process
• Consider incorporating Patient Perspectives
• Integrate FDA input into R&D & Clinical Trial Design

• Advance Regulatory Science by Collaborating with FDA
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